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Isolated corpus callosum lesion associated with cytokine storm in COVID-19

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ABSTRACT

Coronavirus disease 2019 (COVID-19) causes many neurological complications such as cerebrovascular diseases, encephalitis, myelitis, and demyelinated disease. Here we present a rare complication of COVID-19: an isolated cytotoxic lesion of the splenium of the corpus callosum that occurred during a cytokine storm. It responded well to tocilizumab treatment, with complete regression of the lesion.

KEYWORDS Corpus callosum; COVID-19; cytokine storm

Coronavirus disease 2019 (COVID-19) caused by the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially considered a purely respiratory tract infection, but over time has been shown to cause cardiovascular, renal, gastrointestinal, hepatic, hematological, metabolic, and neurological diseases.[1–3] Cerebrovascular diseases, encephalitis, myelitis, demyelinated disease, and inflammatory and immune-mediated neurological damage are seen in SARS-CoV-2 infection.[4,5] We present a patient with a cytotoxic lesion in the splenium of the corpus callosum that occurred during a cytokine storm that developed after diagnosis of COVID-19.

CASE PRESENTATION

A 43-year-old man with no specific medical history presented to the emergency service with signs of fever and upper respiratory tract infection. He had moderate lymphopenia (880 cells/μL) and mild C-reactive protein elevation (22 mg/L). His polymerase chain reaction test was positive for SARS-CoV-2 from a nasopharyngeal swab, and favipiravir treatment was initiated. The patient developed cough, dyspnea, and speech disorder after 5 days. His lymphocyte count was 340 cells/μL; C-reactive protein, 94 mg/L; D-dimer, 2185 μg/L; and fibrinogen, 689 mg/dL. A diffuse ground glass appearance consistent with COVID-19 pneumonia was observed on thoracic computed tomography. On neurological examination, dysarthria was detected, and diffusion restriction was observed in the corpus callosum splenium consistent with cytotoxic edema in diffusion magnetic resonance imaging (MRI). Cranial MRI showed an isointense lesion at T1 and hyperintense lesions in T2 and fluid-attenuated inversion recovery (FLAIR) sections in the splenium of the corpus callosum, without contrast enhancement *(Figure 1)*. No pathology was found in the cerebrospinal fluid except for the protein height (143 mg/dL). Low-molecular-weight heparin and methylprednisolone (250 mg/day) were added to the patient's favipiravir treatment.

Under methylprednisolone treatment, symptoms progressed and the patient presented with ataxia with dysarthria and resistant severe tachypnea. A high serum interleukin-6 level (19.6 pg/mL) was detected. A tocilizumab infusion (total 800 mg) was given to the patient, who was suspected of having cytokine storm based on clinical and laboratory findings. After tocilizumab treatment, the patient showed significant clinical improvement, and laboratory findings began to return to normal values. After discharge on day 40, his neurological examination was normal and MRI revealed total regression of the corpus callosum lesion *(Figure 2)*.

DISCUSSION

There appear to be multiple mechanisms for SARS-CoV-2 to cause neurologic damage, including direct neuronal

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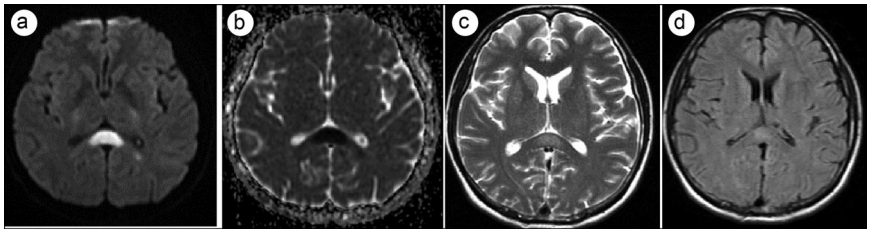

Figure 1. **(a)** Diffusion-weighted imaging and **(b)** apparent diffusion coefficient images show the splenium of the corpus callosum compatible with cytotoxic edema. **(c)** Axial T2 and **(d)** axial FLAIR sequences show a hyperintense lesion.

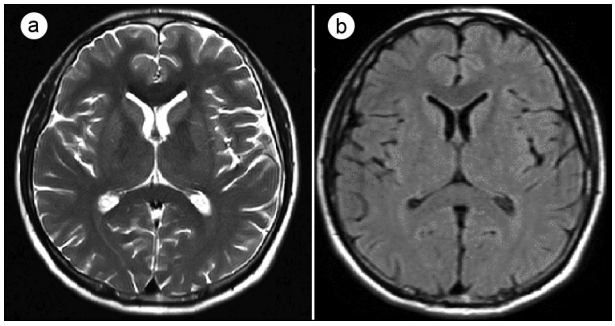

Figure 2. **(a)** Axial T2 and **(b)** axial FLAIR sequences on the 40th day reveal total regression of the corpus callosum lesion.

injury, hypoxic damage from unresolved respiratory distress, autoimmune injury from the induced cytokine storm with resultant blood-brain barrier breakdown, vasculitis, and acute ischemic injury from a hypercoagulable state.[6–8]

Cytotoxic lesions of the corpus callosum have been described by a variety of pathologies, including drug-related conditions, trauma, malignancy, metabolic disorders, and various viruses such as adenovirus, H1N1 influenza, Epstein-Barr, and rotavirus.[9] When cytokine release and inflammation are present in sufficient levels within the brain, astrocytes are stimulated to release glutamate as well as block the reuptake of this neurotransmitter.[9–11] The greatly increased amount of glutamate within the extracellular space leads to excitotoxic action on multiple glutamate receptors, sodium-potassium pumps, and aquaporins, resulting in an influx of water trapped within the cells.[9,12,13] These effects manifest on imaging as diffusion restriction, as seen in our patient. It is believed that the corpus callosum is vulnerable to cytokine-induced injury due to the high density of cytokine, glutamate, and other receptors present within this region of the brain, particularly the splenium.[9,14,15] These previously described mechanisms, combined with our patient's extremely elevated markers for acute-phase reactants, suggest initial autoimmune injury from a cytokine storm. However, it should be kept in mind that both cytokine storm and SARS-CoV-2 infection may also cause ischemia in the splenium. Therefore, anticoagulant therapy should be continued.

Although various neurological complications related to COVID-19 have been reported, this case is presented because of the rare occurrence of an isolated cytotoxic lesion of the splenium of the corpus callosum. It is important to highlight the patient's good response to tocilizumab treatment and complete regression of the lesion.

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